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MURRINA, A TRYPANOSOMAL DISEASE OF EQUINES IN PANAMA.*

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(From the Board of Health Laboratory, Isthmian Canal Commission.)

Murrina is a fatal type of equine trypanosomiasis met with on the Isthmus of Panama. The disease is known throughout the republic by the names "murrina" and "derrengadera," the natives believing that there are two distinct diseases, the one called murrina being a chronic disorder manifesting itself by edema and general weakness, while derrengadera is a disease which may be slow or rapid in its course, but in which there is always paresis of the hind legs and no edema.

The Commission corrals were free from any disorder of this type from 1904 until the middle of 1909, when there broke out among some mules and horses that had recently arrived from the United States and had been pastured with native horses at Gatun, the fatal trypanosomal disease which has been identified as murrina and derrengadera. The clinical features of this disease briefly stated are these: General weakness and droopiness, followed by progressive emaciation, the coat becoming rough and staring. At first there are febrile paroxysms and later an irregular or continued fever, reaching 104° or 106° F., rarely 107° or 108° F. A severe anemia develops, with pallor or a muddy yellow color, and ecchymoses of the nasal and ocular conjunctivae. Toward the end of the disease in some animals a staggering gait was noticed. Extreme emaciation, edema of sheath, lower abdominal wall, or legs were features observed in some animals permitted to die of the disease.

THE DISEASE IN HORSES AND MULES.

Period of incubation.—This was determined experimentally in two animals, pony mule 136 and horse 47. Each animal was inoculated with two or three drops of blood from infected guinea-pigs. The period of incubation in No. 136 was six days, and in No. 47 it was eight days. The end of the period of incubation, or the time of the appearance of trypanosomes in the peripheral blood in numbers sufficient to be detected

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* Received for publication January 25, 1911.

microscopically in a fresh blood specimen, was followed within 24 hours by a sharp rise of temperature from normal (99.5°–100° F.) to 106°+ F.

Duration of disease.—This was determined experimentally in two animals. In horse 10 the period was 54 days after the date of inoculation. In pony mule 136 it was 98 days after the date of inoculation. This mule, however, was treated with arsenic late in the disease, the duration of which was probably not materially altered.

Animals have been kept under observation from the time that symptoms appeared and when trypanosomes were first discovered, until the time of death, and the periods were as follows:

Work horse 121: It is not known when this horse became infected. The duration was at least 73 days and may have been 219 days or more.

Mule 239: Duration 130 days. This animal received arsenic medication late in the course of the disease, the duration of which was probably not materially altered.

Mule 520: Duration of disease, 42 days; in mule 263, 28 days; in mule 257, 18 days; in mule 185, 55 days.

Symptomatology.—While there are several phases or types of the disease, the edematous, wasting, or paretic, they merge into one another, and one phase may follow the other in the same animal. In experimental animals the first indication of the disease is the appearance of trypanosomes in the peripheral blood; this is followed in 24 hours by a rise in temperature to 105° or 106° F. In the corrals, however, the first indication of the disease would be general weakness and inability to do the accustomed work. The coat becomes staring, and in some animals a conjunctivitis with considerable secretion of muco-serous fluid would be seen. The weakness appeared oftenest to be a general one associated with wasting of flanks and haunches. When the animals were exercised their gait was slow, and sometimes a trace of clumsiness in the co-ordination of the hind legs would be noted. A few animals lost rapidly in weight and died within a few days. Others would linger for several weeks, maintaining good appetites, but becoming thinner each day. Edema of the hocks, or legs, the sheath or dependent portions of the belly, appeared in some animals, generally to disappear and to be followed by further emaciation. Some animals toward the close of the disease, whether of long or short duration, and generally during a febrile paroxysm, would hang their heads as though drowsy. A few days before death they would either lean against the stall or would fall down and be unable to rise, though in some instances if helped up they could frequently stand for a day or two. One mule was down four days before he died. One horse died in a sitting posture, his hind legs being placed in a peculiar outstretched position.

The temperature has been recorded in most animals. It shows a marked tendency toward relapses, as in recurrent fever; though sometimes the febrile paroxysms in which the temperature was 103–105° F. were replaced by an elevated continued fever lasting from 3 to 22 days. The temperature at times was irregularly quotidian. On the whole the temperature was elevated during the period when trypanosomes were visible microscopically in the peripheral blood, but the trypanosomes appear before the temperature rises and generally disappear before the temperature reaches normal. The animal is inclined to be droopy during a febrile paroxysm and brightens after the crisis.

There is a progressive and severe anemia. The red blood cells early in the disease, even before trypanosomes appear in the peripheral blood, show a tendency to clump, not in rouloux, but in small and large masses. During the course of the disease the red cells may be reduced to 2,500,000 per c.mm., or less. The blood clots rapidly. There is a lymphocytosis. The anemia is shown in the muddy pallor of the conjunctivae and nasal mucosae. Petechial hemorrhages are seen in the conjunctivae and nasal mucosae late in the disease and are valuable aids to diagnosis in the corrals.

Trypanosomes are no doubt always present in the peripheral blood, for susceptible animals may be infected with the blood of sick animals when trypanosomes are apparently absent by ordinary microscopic examinations.

In several cases trypanosomes would appear for one, two, three, or more days, to disappear for two to nine or more days. When present in greatest numbers there are approximately 600 per cubic millimeter. Usually there are much less than this.

In some of the animals, as the end approaches, there is a definite paresis of the hind quarters, with inability to stand or co-ordinate the movements of the hind legs. This has appeared in from one to six days before death.

Abstracts of records.—Horse 121: Arrived on the Isthmus April, 1909; pastured and worked at Gatun, and possibly infected there. His leg was fractured and later he was condemned and sent to Ancon, from Gatun, September 28, 1909. On November 23 he was inoculated with a porcelain filtrate from mule 545 that died at Gatun corral November 22 with symptoms resembling trypanosomiasis, but whose blood just before death contained no trypanosomes upon microscopic examination (Dr. Williamson). There were occasional rises of temperature and unimpaired appetite but slowly progressive loss of weight. Trypanosomes were present in the blood almost continuously until the day of death. They were present when the temperature was elevated and also when it was normal. Edema of the sheath and dependent belly-wall was noticed April 23, and at this time there was perceptible weakness of the left hind leg on walking the animal about. May 4 the horse was down on his haunches, while the swelling of the sheath and belly-wall had disappeared. The horse died during the night of May 7 in a sitting posture, leaning against the wall with his hind legs outstretched to one side.

Mule 228 had been at the Ancon corral continuously for two years. The animal's temperature had been elevated for several days when one trypanosome was found in the blood on the fourth daily examination. There was loss of appetite for three or four days at the onset of the disease. The animal was well nourished but was droopy and his coat was staring. There was also a discharge of muco-purulent fluid from the conjunctivae. On March 26 he was down but was able to rise. Two days later he fell down again and could not be raised; killed. This was an acute case in an animal whose blood contained very few trypanosomes and who died without there being any emaciation.

Mule 382: This animal had worked in the team with mule 204 that died of murrina July 11. On March 23, when he was taken out very sick, his blood contained one trypanosome to one film. His hind legs were outstanding and he was "pulling back on the halter." He became emaciated without edema and was shot.

Mule 185: This animal had been at the Ancon corral for four years, save for a short period, one year ago, when he was worked at Cristobal. On March 30 he fell while at work. His appetite was good but he was somewhat thin, and his blood on this day contained a few trypanosomes in one film. Later he became very much emaciated and died May 25.

Mule 204: This animal had worked in team with infected mule 382, and was no doubt infected from him. He was taken out March 28. Trypanosomes were detected four days later. He became emaciated and on April 11 fell down in the stall and had a general convulsion. On April 13 he was slung in the stall, but on April 26, when removed from the sling, he fell to the floor, unable to rise, and was shot.

Mule 292: This mule had been on the Isthmus four years and seems to have shown considerable resistance to the disease. Some time before routine blood examinations were begun it had been observed at the Ancon corral that this mule was unaccountably weak. He was shipped to San Pablo but was too weak to work there. Later he was sent to Gatun, where he spent most of his time in the sick corral. Finally he was returned to Ancon, where he was put to work, but had to be taken out on account of weakness. Trypanosomes were discovered on the second daily examination, March 31. This animal fell down several times but was always able to regain his legs. Shot, May 12.

SUMMARY OF SUSCEPTIBLE ANIMALS.

Animal	Infected	Result
Work horse	Yes	Died
Mule	Yes	Died
Saddle horse (experimental infection)	Yes	Died
Calf	No	Refractory
Pig	Yes	Recovered
Dog	Yes	Died
Raccoon	Yes	Died
Cat	Yes	Recovered
Kitten	Yes	Died
Monkey *Cebus* and *Nyctipithecus*	Yes	Died
Rabbit	Yes	Died
Guinea-pig	Yes	Died
Rat, *M. rattus*	Yes	Died. Two recovered
Rat, *M. norvegicus*	Yes	Died
Rat, *M. alexandrinus*	Yes	Died. One refractory
Rat, albino	Yes	Died
Mouse, *M. musculus*	Yes	Died
Mouse, albino	Yes	Died
Opossum	Yes	Died
Agouti	Yes	Recovered
Coati	Yes	Died

Work horses and mules were the only equines found infected naturally. Saddle horses were not infected naturally.

Dogs are very susceptible and the disease runs a fairly rapid and fatal course.

Dog 121—2: April 7, large dog, weight 50 pounds, inoculated subcutaneously with two drops of blood in citrated saline solution from guinea-pig 121—1. The period of incubation was less than nine days. On May 12 the anterior chamber of each eye became very turbid, and the lids nearly closed on account of photophobia. He died on May 15, 38 days after inoculation.

Cats are susceptible but recover. On April 7 an adult cat was inoculated subcutaneously with two drops of infected blood in citrated saline solution from guinea-pig 121—1. Trypanosomes were always found in the peripheral blood at intervals up to June 19. On this date the animal had improved in appearance and condition, but had a dermatitis of both ears. The cat's blood has been negative for trypanosomes since June 19.

A very young kitten proved very susceptible. On April 7 the kitten was inoculated from guinea-pig 121—1. On April 15 a few trypanosomes were detected, the period of incubation being 8 days. Trypanosomes were very numerous April 19. The next day the kitten was sick and droopy and died April 21, 14 days after inoculation.

Monkeys are very susceptible. Cebus, 121—1, inoculated subcutaneously with 4 c.c. of blood direct from horse 121 when his blood contained two trypanosomes to one cover-slip. The period of incubation was less than 12 days. Trypanosomes appeared at intervals, becoming very numerous toward the end, when the blood was thin and pale. The animal became very pale and feeble and died 43 days after inoculation.

Nyctipithecus was inoculated from a guinea-pig. The period of incubation was five days. The animal became very feeble and dull. There was diarrhea. A week before death photophobia was noticed and a few days later the anterior chamber of each eye contained flakes of grayish exudation. The animal died 32 days after inoculation.

Rabbits 121—1, A and B (bred in the United States; on Isthmus 3 or 4 mos.): The period of incubation was 12 days or less. Trypanosomes were detected but once, yet each animal developed a severe dermatitis of the muzzle and ears, with blepharitis and conjunctivitis. Later there was loss of hair from the muzzle. One rabbit died 106 days, the other 163 days after inoculation.

In guinea-pigs the period of incubation was about 7 days. Trypanosomes appeared at intervals in numbers up to 10 or 20 to one immersion field. The red blood cells were clumped in the characteristic manner. Swelling of ears with dermatitis, edema and ulceration of scrotum, and edema of vulva were frequently seen. The duration of the disease was 27, 50, 75, 99, 119, 189, and 336 days after inoculation.

Agouti (Conejo): Inoculated with richly infected blood from guinea-pig 121—1. Trypanosomes appeared after 10 days. They then disappeared and were not detected on 11 subsequent examinations, and the animal has remained perfectly normal.

Opossum: Trypanosomes were detected when the animal was very sick. The animal died 34 days after inoculation.

Raccoon 10—2: His blood was examined once, when two trypanosomes were found to one immersion field. Died 52 days after inoculation.

Coati 382—2: Period of incubation six days. Died 24 days after inoculation.

Wild rats, *M. rattus*, are susceptible. Two were inoculated, whose blood contained *T. lewisi*. After several days *T. hippicum* could be detected along side of *T. lewisi* in stained films, but subsequently *T. hippicum* disappeared from the animal's blood, while *T. lewisi* remained present. Both animals recovered.

Two other specimens of *M. rattus* were inoculated, from guinea-pig 10. Trypanosomes appeared in their blood in enormous numbers, and nine days after inoculation they were dying and were killed. It is interesting to note that in neither animal could *T. lewisi* be demonstrated. This suggests the possibility of a vicarious immunization by *T. lewisi*.

M. alexandrinus: Two specimens have been inoculated. In each case their blood was negative for *T. lewisi*. One died 11 days after inoculation. The other never became infected.

M. norvegicus: One specimen inoculated September 22 from white mouse 10—2. Trypanosomes were present for several days, were absent on October 10, reappeared October 13, and the rat died November 1, 40 days after inoculation.

Rat, albino: These animals are somewhat more susceptible than wild rats. In white rat 382—2 enormous numbers of trypanosomes appeared and the animal died 20 days after inoculation.

The wild mouse, *M. musculus*, was very susceptible. Trypanosomes appeared five days after inoculation in numbers of from 1 to 25 fields up to 12 to 1 field. They remained constantly in the blood in increasing numbers until they were more numerous than the red blood cells. The animals then died, 8, 9, 12, and 15 days after inoculation.

White mice were very susceptible. The period of incubation was from three to five days, some of the animals dying on the eighth day.

Fig: This animal is susceptible but recovers. Pig 382—2 was inoculated April 13 with blood from guinea-pig 382—1. Trypanosomes were detected on one occasion, April 28. They then disappeared and were never found again. The red blood cells were never clumped. The animal increased rapidly in weight and was perfectly well when killed June 29.

A calf was refractory. Calf 121—2 inoculated April 3 with 10 minims richly infected blood from Cebus 121—1. Trypanosomes could never be detected in the animal's blood in 17 examinations during three subsequent months, and his temperature remained normal during this period. The calf increased in weight and his condition greatly improved. On July 6, 2 c.c. of his blood were inoculated into a young guinea-pig, but trypanosomes have never appeared in the guinea-pig's blood.

PATHOLOGICAL ANATOMY OF MURRINA.

When a horse is sacrificed before the disease has run its course there may be very few gross lesions and none characteristic of the disease other than emaciation, edema of lower belly-wall, sheath or legs, excessive fluid in some of the cavities, conjunctival ecchymoses, or some splenic enlargement. If, however, the animal is permitted to die naturally there are lesions which are characteristic and usually well marked.

The spleen is only slightly enlarged, but its capsule, particularly the external surface, is dotted over with petechiae limited to the capsule. They are usually one to two mm. in diameter. The recent ones are bright red, while those somewhat older are reddish-brown in color. The pulp is only slightly increased and the reticulum is unchanged.

The kidneys contain punctate petechiae, one mm. in diameter, distributed chiefly in the cortex, just beneath the capsule.

The endocardium and epicardium usually contain large and small hemorrhages. Favorite sites are the papillary muscle, mitral leaflets, and the epicardial fat along the coronary arteries, oftenest near the base of the heart.

The pleurae and peritoneum in some cases have been the seat of numerous petechiae.

The renal lymph nodes are usually enlarged, and one or two of the set are frequently the seat of extensive hemorrhages.

There are usually hemorrhages into the conjunctival or nasal mucosae seen at some time during the disease.

Sometimes there is an excess of clear, serous fluid in the peritoneum, pleural, or pericardial cavities, but this is not constant, nor is the edema of the sheath, legs, hocks, or lower belly-wall constant.

Other viscera show no changes.

Filaria and intestinal nematodes and cestodes were encountered inconstantly.

The microscopic changes are fairly characteristic and constant. In the kidneys the focal hemorrhages and the acute glomerulitis, occasionally with necroses, make a rather striking picture. The spleen always shows the same appearance—phagocytosis of red blood cells and the presence of blood pigment in small and large clumps of refractile granules. In the liver the one unvarying feature is the presence of bronze-colored blood pigment in the endothelial cells of the sinusoids. There is a localized leukocytosis here. Atrophy and fatty infiltration of the hepatic cells are inconstant and not definitely related to the disease process. Renal lymph nodes usually show great engorgement, hemorrhage, and phagocytosis of red blood cells by large mononuclear phagocytes. The hemorrhages in other viscera present nothing of special interest.

IMMUNITY.

Embryos are not infected through the placenta (guinea-pigs), nor does an infected mother confer any immunity upon her offspring *in utero* as indicated by the result of the following experiment:

A gravid guinea-pig was inoculated with trypanosomes April 11. One young pig was born April 26, 15 days after the inoculation of the mother. The blood of the young guinea-pig, on examination, contained no trypanosomes, although the mother had a severe infection and died 99 days after inoculation. To ascertain whether there was any immunity conferred on the young, she was inoculated May 10 from guinea-pig 382, and trypanosomes appeared after a latent period of eight days.

DIAGNOSIS.

The diagnosis is made by the detection of weak animals "pulling back on the halter" or those with outstanding hind legs, animals temporarily off their feed, or those that in spite of sufficient food show steady physical deterioration. With these symptoms there may be conjunctivitis, anemia, and subconjunctival ecchymoses. As soon as such an animal shows a temperature of 101° F. or more, a blood examination will generally reveal the trypanosome; particularly if the elevated temperature is detected at the beginning of the access. During the latter part of the paroxysm trypanosomes may not be demonstrable. The inoculation of very susceptible animals, such as mice, rats, monkeys, dogs, or guinea-pigs, will help in making a diagnosis in some of the cases or on some occasions when trypanosomes are extremely sparse in the peripheral blood.

In obtaining blood from the ear for diagnosis, no time should be lost before examining fresh cover-slip preparations, for occasionally the trypanosomes lose their motility within a few minutes after the blood is drawn, and can then only be detected in stained specimens. It has occurred not infrequently that what apparently were negative fresh preparations contained trypanosomes after staining. Trypanosomes commonly remain for a time within a clump of red cells, which can be seen to be disturbed, yet it is often impossible to detect for a minute or two the hidden trypanosome. Ross's thick-film method, or a modification in which half the drop is thinned out on the slide in order to detect morphological features, is of value in detecting trypanosomes when they are very sparse.

THE PATHOGENIC AGENT.

The pathogenic agent is *Trypanosoma hippicum*[1] nv. sp.

While there is some variation in its morphology, the typical trypanosome is 16 to 18 mikrons in length, two mikrons wide, the distance from kinetonucleus to the posterior tip about 1.75 mikrons, and the distance from the posterior tip to the middle of the trophonucleus is from 7.5 to 10 mikrons. The flagellum is usually short and frequently not entirely free, for often the attenuated process of the cytoplasm extends to the extreme end of the chromatin filament; but at times there is a free flagellum reaching 4 mikrons in length. The trophonucleus is placed a little posterior to the middle, the relation being 1:2.8 to 1:2.4. The kinetonucleus is usually placed about 1.75 mikrons from the posterior

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[1] *Bull. Soc. Path. Exot.*, 1910, 3, and 1911, 3.

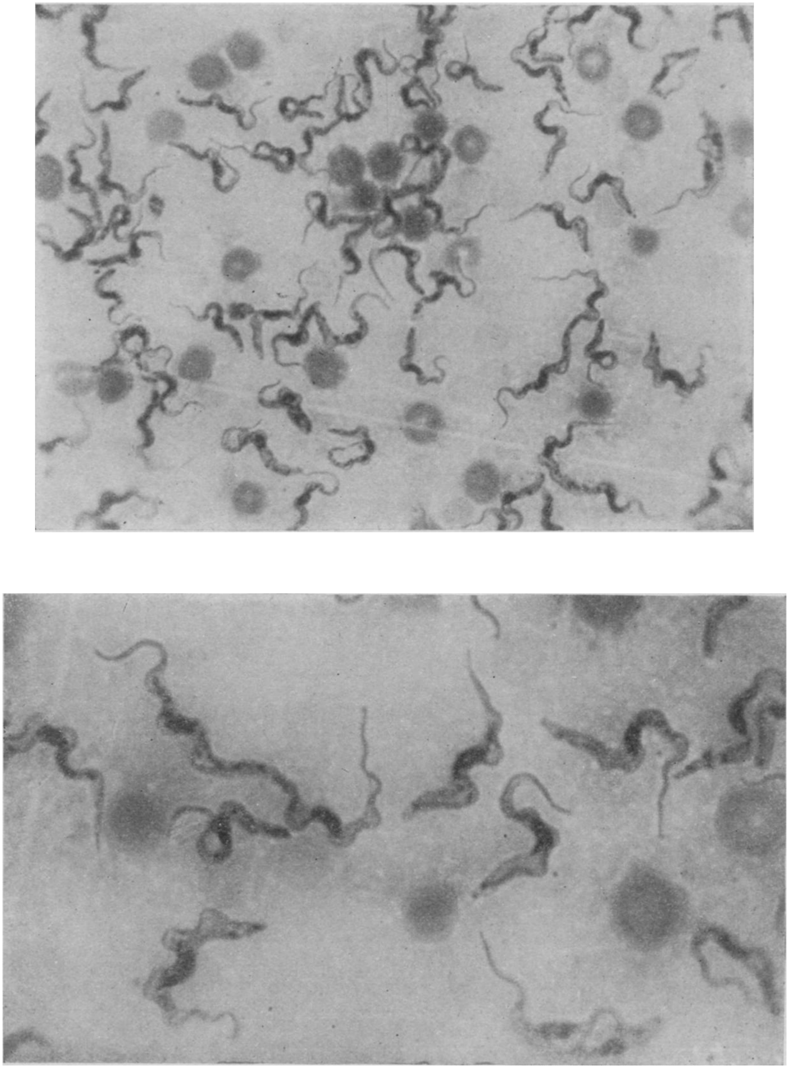

FIG. 1.—*T. hippicum* from rat.

tip; but sometimes it is quite at the tip, and occasionally may be 3 mikrons from it. The posterior tip is often rather blunt and usually obtuse, never being as attenuated as the posterior tip of *T. lewisi.* The cytoplasm usually contains numerous basophilic granules scattered throughout the cytoplasm or arranged in lines in the anterior and posterior halves. The granules are coarse and from 0.5 to 1 mikrons or more in diameter. There may be 16 to 18 in number, most of them being placed, usually, in the anterior half. The lateral margin of the trypanosome may stain more deeply than the interior. Some of the longer forms contain few or no granules. A well-developed undulating membrane is present and the chromatin filament extends from the kinetonucleus to the anterior tip of the flagellum. When rapidly proliferating in the rat or mouse some forms approach 28 mikrons in length, and become 3 to 4 mikrons in width. From this description it is quite evident that the trypanosome is different from *T. equinum* of mal de caderas, and *T. equiperdum* of dourine. Dr. Laveran, who very kindly has examined preparations of the trypanosome, has expressed his opinion that *T. hippicum* differs from the two above named trypanosomes by the presence of a centrosome, basophilic granulations, and in having a short flagellum. "Les centrosomes sont très apparents; il ne s'agit donc pas du trypanosome du mal de caderas. D'autre part le trypanosome me parait différer notablement du *Tr. équiperdum:* il est plus petit; le partie libre du flagelle est plus courte, enfin le protoplasme contient des granulations basophiles qui sont presque toujours défaut chez le *Tr. équiperdum.* Le fait que les singes et les cobayes s'enfectent facilement est aussi contraire au diagnostic de dourine."[1]

There is some variability in the presence and in the staining qualities of the basophilic granulations. Some specimens from the horse would have few or no granulations, while others had several deeply staining ones. One film from *M. alexandrinus* had many trypanosomes and none contained granules, though the cytoplasm stained deeply; from the same rat there were other specimens containing many well-stained granulations. It has appeared at times as though when the trypanosomes were multiplying very rapidly they were longer, more attenuated, and freer from granules. The process of division appears from an examination of peripheral blood smears to take place, first, by division of the kinetonucleus, then the development of a second faint chromatin filament from the second kinetonucleus, later a division of the trophonucleus, and finally a separation of the two trypanosomes.

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[1] See also *Bull. Soc. Path. Exot.*, 1911, 4. p. 168.

Trypanosomes do not die within at least 10 minutes in the drawn blood of animals to which has been added 90 per cent by volume of citrated saline solution, 0.9 per cent sodium chloride in 1.5 per cent sodium citrate solution. Inoculations, therefore, can be made with the aid of this fluid.

MODE OF TRANSMISSION.

A study of this phase of the disease impresses one very strongly that it is carried mechanically by flies. The pasture at Gatun, where the infection was supposed to have been introduced, was visited on several occasions, but tabanid flies were not found there. This pasture is not near the woods, and questions put to the corral men elicited the information that tabanids have not been seen in that locality. While they are present on the Isthmus, they do not seem to be thickly nor widely distributed. In the bush and mountains near streams they are said to be common in some places. A few were taken in August, 1909, at the new Ancon corral, and a few have been caught at the isolation corral near by, where the infected animals have been kept. None were ever taken at the old corral where the disease first appeared.

Stomoxys calcitrans naturally is found wherever horse manure is exposed. It is customary here to remove manure every 24 hours from the corrals: however, as it is not destroyed, but used for fertilizing purposes, flies are not prevented from breeding, and *S. calcitrans* has been bred out at the Laboratory from corral manure exposed on plant beds. *S. calcitrans* containing blood has been taken at Ancon corral and at the isolation corral where the infected horses were kept. Other flies taken at the stables or near by, during autopsies on mules, were representatives of Compsomyia, Hylemyia, Musca, and Pyrellia.

Tabanids cannot be held responsible for the transmission of this disease, because the infection has spread in certain localities where apparently tabanids never visit.

While it is possible that *S. calcitrans* may have conveyed the infection by biting, it is extremely unlikely for the following reasons:

In the isolation corral at Ancon, which had been unscreened for four months and in which *S. calcitrans* was breeding, there were two animals, a horse and mule, infected with *T. hippicum*, standing alongside a pony that did not contract the disease, though the contact with these infected animals and with several others lasted altogether 10 months. At the end of this period the pony was inoculated with trypanosomes experimentally to determine his susceptibility, and he developed a severe infection in eight days (horse 47).

Similarly, at the old Ancon corral, from which several of the infected mules were taken, there were two long rows of stalls. On the outside, facing the roadway, the saddle horses were stalled, about 18 or 20 being kept there constantly. On the other side was a row of stalls occupied by work mules, from which several sick animals, suffering from murrina, were taken out and for several days segregated at one end of the row. The stalls were covered with a roof, but were not screened or protected in any other way. The mangers and hay racks came together so that only a few inches of partly open space separated the horses' and mules' heads. *S. calcitrans* was breeding in the corral at this time and several specimens were taken alive with mule's or horse's blood in their intestinal tracts. The period of exposure of the saddle horses in this way lasted at least six months, yet no saddle horse ever became infected with trypanosomes from the mules near by, though mules kept coming down with the infection during this same period.

A horse (No. 10) and a mule (No. 136) with intact skins kept in this corral with the other animals for one month showed no signs of infection, though both were susceptible, as subsequent inoculation experiments proved.

Furthermore, specimens of *S. calcitrans*, from this infected corral, were dissected and others fed from infected horses, yet no evidences of flagellates were ever detected in their intestinal tracts.

It is extremely unlikely, therefore, that *S. calcitrans* transmitted the disease by biting.

Another possible mode of transmission was that of ticks, but upon investigation it was found that the only animals harboring ticks were saddle horses that had been taken out on trails into the bush. Ticks could never be collected from corral mules, naturally, because they did not visit places infested with *Dermacentor nitens*, *Margaropus annulatus*, and *Amblyomma cajennense*, the ticks most commonly found on horses in this region. Now as none of the saddle horses ever became infected with trypanosomes, though stalled alongside infected mules in an unprotected stable, it became evident that ticks did not transmit the infection.

Before the isolation corral was screened, bats visited it and bit one of the infected horses on several occasions on both sides of the neck. Curiously enough, this was the only animal out of three or four in the stable that was bitten. While bats under such circumstances might open a channel for infection by breaking the skin of an infected animal and permitting flies to become infected, it did not seem that in this case, at any rate, they transmitted the infection: but if they had visited non-immune horses and bitten them immediately after visiting and biting an infected horse, the bats would have then possibly become a transferring medium.

None of the bats taken here have been infected with trypanosomes, though filariasis is very common.

It finally appeared from an examination of the infected animals and the nature of the work they had been doing that no matter how the infection crept into the corrals in the first place, it was subsequently transmitted mechanically by flies visiting the galls and scraper cuts of infected and non-infected animals. The infected animals were always work animals, many of them being placed on the hardest kind of work—scrapers—and were always being laid up with cuts and abrasions received in this way. The mules and horses that preserved intact skins probably never became infected. There were two positive cases of infection in mules that had been driven together in team, and it is understood that there were four or six others, but the information is not positive. It seemed right, then, to assume that flies were the active agents in transmitting the infection, and that they conveyed it mechanically.

TREATMENT.

Prophylaxis.—The likelihood of this assumption seems to have been borne out by the result of treatment which was instituted, and which apparently has resulted in saving the work horses from further infection. Twenty-three animals, at least, had been destroyed by this disease between April, 1909, and April, 1910.

The following recommendations were made and largely carried out with the result that the epidemic has been completely wiped out:

1. Destruction of all infected animals and burial away from the corral to prevent flies becoming infected from blood at the time of shooting, if near the corral.
2. Routine daily (b. d.) temperatures for the detection of suspects.
3. The isolation in screened, vestibuled, fly-proof stables of all animals having a temperature above 100° F.
4. The detection of infected animals by blood examinations, and animal inoculations when necessary.
5. The disinfection of halters, instruments, etc., and the hands of attendants coming in contact with infected animals.
6. All wounds, sores, galls, etc., on well, infected, living, or dead animals to be protected from flies by protective dressings, containing substances such as creolin, distastful to flies.
7. Stray horses and mules are not to be impounded in or near corrals.
8. Sanitary inspectors and police are required to report all animals having this disease.

Arsenic medication.—This subject is being pursued by means of the administration of large subtoxic tertian doses of arsenious oxide (Holmes's method) to experimentally infected mules and horses, and as the work is not completed it will be made the subject of a separate report.

SPECIFIC IDENTITY OF THE DISEASE AND ITS DIFFERENTIATION FROM OTHER FORMS OF EQUINE TRYPANOSOMIASIS.

It is necessary to establish the fact that murrina is a specific disease, distinct from other forms of equine trypanosomiasis.

From the total number known to science of trypanosomes invading mammals, those of rodents, cattle, bats, etc., may at once be dismissed from consideration, as they are not pathogenic for equines, viz., *T. lewisi*, *T. Theileri*, etc.

The following trypanosomes may also be dismissed from consideration for the reason that they are either pathogenic for cattle or present well marked morphological and other points of difference from *T. hippicum: T. evansi*, *T. brucei*, *T. dimorphon*, *T. pecaudi*, and *T. cazalboui*.

T. equiperdum, the pathogenic agent of dourine (mal de coit) is differentiated by morphology, it containing no basophilic granulations, by the fact that it is extremely rare in the peripheral blood of equines and further by clinical features, mode of transmission, dourine being a disease transmitted during copulation; and further by the insusceptibility of monkeys and guinea-pigs to *T. equiperdum*.

There remains one trypanosome which must be carefully differentiated from *T. hippicum*. That one is *T. equinum*, the pathogenic agent of mal de caderas. Dr. Laveran's opinion has already been quoted. In addition to this valuable testimony we will consider what other characters may be discovered in the two diseases which may be used to differentiate them.

Mal de caderas is an epizoötic trypanosomal disease of equines in South America. The trypanosome was discovered by Dr. Elmassian,[1] director of the Bacteriological Institute at Assomption, Paraguay, in 1901. Geographically, the disease is distributed in regions along the tributaries of the Rio de la Plata in Argentina, Uruguay, Paraguay, Brazil, and Bolivia, and also in the federal district of Matto Grosso, between the Madeira and Xingu rivers, tributaries of the Amazon in Brazil, and on the Island of Marajo at the mouth of the Amazon.

Certain clinical and pathological features are mentioned by

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[1] Elmassian, *Rev. Soc. med. Argent.*, 1902, 10, p. 122.

Elmassian and Migone, Voges, Laveran, and Mesnil, as being more or less characteristic of mal de caderas. It should be mentioned, however, that there is much similarity among all equine trypanosomal diseases—that they, varying from one another, usually present certain characters recognizable as belonging to the type—symptom and pathological group—such as anemia, emaciation, edema, effusions, posterior paresis, hemorrhagic nephritis, and remittent pyrexia. Furthermore, if we take one disorder and observe all its vagaries, we shall see that each individual case does not necessarily conform to the specific disease type.

In mal de caderas the characteristic symptom would seem to be, as its name implies, posterior paresis, yet as Voges points out, in a series of cases unusual forms present themselves—"a number of animals may remain quietly standing up to the last moment and then fall in a heap and die at once."

The fairly constant features in which murrina differs from mal de caderas seem to be these:

Duration of disease in mules and horses.—Murrina is far more common among mules than horses. This has been undoubtedly due to the nature of the mules' work here, rendering them more liable to infection through cuts and galls. The duration of the disease is the same in mules and horses. The longest duration recorded is in a horse. According to Voges the duration of mal de caderas in horses is one to two months, occasionally four months, while in mules it is one year, if they receive good care and treatment. This is quite different from my observations of murrina.

The number of trypanosomes in the blood of mules and horses.—The blood of several mules suffering from murrina has been examined daily over periods of several weeks or months and trypansomes were easily found at intervals, particularly before and during a febrile paroxysm. Voges states, however, that in mal de caderas trypanosomes cannot be demonstrated microscopically in the blood of mules suffering from the disease for days and weeks. In one case, he states, after two months daily diligent examination, trypanosomes were found only once during an attack, and in numbers much less than in the horse. In another case, trypanosomes were only found on two days during the duration of the disease in a mule. In murrina no difficulty has ever been experienced in detecting trypanosomes in mules if the examinations were made during a febrile paroxysm; and trypanosomes are also frequently found when the temperature is normal. Furthermore, the blood of infected horses has never been found to contain more trypanosomes than that of infected mules.

Character of fever.—A very exact idea of the type of fever in mal de caderas could not be obtained for the reason that most of the published charts are based on single daily temperature records. There appears, however, to be no very marked differences in the types of fever between murrina and mal de caderas.

Elmassian has described placques of dermatitis on the neck, shoulders, and rump of horses in mal de caderas, but these have never been observed in cases of murrina.

Keratitis and hypopyon are mentioned as being seen in horses infected with *T. equinum*, but neither of these conditions has been observed in horses or mules suffering from murrina.

Diarrhea, said to be a common symptom in mal de caderas, according to Elmassian, has not been observed in murrina, save in one horse that had received 21 gms. of arsenic.

Hemoglobinuria and hematuria have never been observed in cases of murrina. If they were at all common it would have been noticed, for all the animals have been kept under observation by the veterinarian in the corrals. These sypmtoms are said to be constant in mal de caderas.

Distinguishing pathological features of murrina.—These are very important means of differentiating the two diseases. They are as follows: splenic capsular ecchymoses; renal petechiae; epicardial and endocardial hemorrhages and ecchymoses, and less frequently pleural and peritoneal petechiae. These, with the hemorrhages into the renal lymph nodes, make up a picture quite different from mal de caderas, and one more like nagana and "equine anemia."

The spleen is not greatly enlarged in murrina but always appears to be so in mal de caderas.

Fibrinous exudation into the pleural and pericardial cavities described as constant in mal de caderas is very rarely seen in murrina (there was a fibrinous clot in the right pleural cavity of mule 263).

SUMMARY.

There has been an epidemic of trypanosomiasis among American mules and work horses in the Canal Zone. The disease resembled other trypanosomal diseases such as nagana, surra, mal de caderas, and Senegambian horse disease; but it presented a group of symptoms and pathological features which stamp it as a distinct disease.

The disease is differentiated from mal de caderas by the morphological characters of the trypanosome, the autopsy picture, and the clinical features of the disease.

The disease also resembles in some particulars "swamp fever" or the "infectious anemia of equines," a disease of obscure etiology, prevalent in some parts of the western United States.

The disease was probably not introduced from outside sources, but represents an endemic disease of this region, known in the Republic of Panama as murrina and derrengadera.

It is distinctly a disease of mules and horses, for cattle are insusceptible.

The pathogenic agent, *T. hippicum*, has morphological and biological characters which differentiate it from other species of trypanosomes.

The animal reactions of several of the native mammals, including domestic animals, have been determined.

The chief distinguishing features of the disease are: anemia; weakness; emaciation and edema; conjunctival ecchymoses; conjunctivitis; pyrexia, and some posterior paresis. The pathological findings are constant and characteristic: splenic capsular ecchymoses; acute hemorrhagic nephritis, with acute glomerulitis and petechiae; hemorrhages in renal lymph nodes; epicardial and endocardial ecchymoses, and less constantly pleural, peritoneal, and conjunctival ecchymoses, and pleural effusion. The blood changes are those of anemia with lymphocytosis. There is much phagocytosis of blood pigment by endothelial cells of the liver and spleen.

The disease is probably transmitted mechanically by flies through the broken skin of cuts and various wounds. Saddle horses were not infected, and there are no evidences that any

animals were infected by means of stomoxys or tabanids or by ticks or bats.

The epidemic, which threatened to destroy several hundred mules and horses, has been controlled (there having been no new case in six months) by detection of infected animals, by means of daily routine temperature records throughout the corral, the microscopic examination of the blood of all animals having a temperature above 100° F., the isolation in screened stables of infected animals or suspects, and the sacrifice of all infected animals.

I wish to express my thanks to Lieutenant-Colonel C. A. Devol, U.S.A., Lieutenant W. E. Wood, U.S.A., and others in the Quartermaster's Department for various courtesies and help.

I am indebted to Dr. L. B. Bates for help with autopsies, and for keeping up the examinations of experimental animals, etc., while I was on leave, and to Colonel W. C. Gorgas, U.S.A., for permission to publish.